

## § 316.12

## 21 CFR Ch. I (4–1–12 Edition)

(iii) So far as is known or can be determined, all indications previously or currently under investigation anywhere;

(iv) All adverse regulatory actions taken by the United States or foreign authorities.

(8) The basis for concluding that the drug is for a disease or condition that is rare in the United States, including the following:

(i) The size and other known demographic characteristics of the patient population affected and the source of this information.

(ii) For drugs intended for diseases or conditions affecting 200,000 or more people in the United States, or for a vaccine, diagnostic drug, or preventive drug that would be given to 200,000 or more persons per year, a summary of the sponsor's basis for believing that the disease or condition described in paragraph (b)(6) of this section occurs so infrequently that there is no reasonable expectation that the costs of drug development and marketing will be recovered in future sales of the drug in the United States. The estimated costs and sales data should be submitted as provided for in § 316.21(c).

(9) A summary and analysis of available data on the pharmacologic effects of the drug.

(10) A summary and analysis of available nonclinical and clinical data pertinent to the drug and the disease to be studied including copies of pertinent published reports. When a drug proposed for orphan drug designation is intended to treat a life-threatening or severely debilitating illness, especially where no satisfactory alternative therapy exists, the sponsor may wish voluntarily to provide this information. A sponsor of such a drug may be entitled to expeditious development, evaluation, and marketing under 21 CFR part 312, subpart E.

(11) An explanation of how the data summarized and analyzed under paragraphs (b)(9) and (b)(10) of this section support the rationale for use of the drug in the rare disease or condition.

(12) A definition of the population from which subjects will be identified for clinical trials, if known.

(13) A detailed outline of any protocols under which the drug has been or

is being studied for the rare disease or condition and a summary and analysis of any available data from such studies.

(14) The sponsor's proposal as to the scope of nonclinical and clinical investigations needed to establish the safety and effectiveness of the drug.

(15) Detailed protocols for each proposed United States or foreign clinical investigation, if available.

(16) Specific questions to be addressed by FDA in its recommendations for nonclinical laboratory studies and clinical investigations.

[57 FR 62085, Dec. 29, 1992; 58 FR 6167, Jan. 26, 1993]

### § 316.12 Providing written recommendations.

(a) FDA will provide the sponsor with written recommendations concerning the nonclinical laboratory studies and clinical investigations necessary for approval of a marketing application if none of the reasons described in § 316.14 for refusing to do so applies.

(b) When a sponsor seeks written recommendations at a stage of drug development at which advice on any clinical investigations, or on particular investigations would be premature, FDA's response may be limited to written recommendations concerning only nonclinical laboratory studies, or only certain of the clinical studies (e.g., Phase 1 studies as described in § 312.21 of this chapter). Prior to providing written recommendations for the clinical investigations required to achieve marketing approval, FDA may require that the results of the nonclinical laboratory studies or completed early clinical studies be submitted to FDA for agency review.

### § 316.14 Refusal to provide written recommendations.

(a) FDA may refuse to provide written recommendations concerning the nonclinical laboratory studies and clinical investigations necessary for approval of a marketing application for any of the following reasons:

(1) The information required to be submitted by § 316.10(b) has not been submitted, or the information submitted is incomplete.